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PILLSBURY WINTHROP SHAW PITTMAN, LLP
P.O. BOX 10500
MCLEAN, VA 22102

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/936,333
Filing Date: March 05, 2002
Appellant(s): DICKSON ET AL.

Thomas A. Cawley, Jr, and Charles C. P. Rories
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed November 28, 2006 appealing from the Office action mailed August 10, 2005.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows:

WITHDRAWN REJECTIONS

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner. The second ground of rejection was withdrawn in the Advisory action of November 30, 2005. The third ground of rejection identified by the Appellant (rejection of claim 36 for lacking adequate support for antibodies that bind to matriptase complex with any Kunitz-type serine receptor) is moot in view of the After-Final amendment of

November 8, 2005 limiting claim 36 to embodiments wherein matriptase is in complex with HAI-1.

NOT A REJECTION OF RECORD

The Fourth ground of rejection presented by the Appellant is not a basis of rejection of record. While Appellant correctly indicated that claim 36 was independently evaluated for rejection for lack of written description as above (in the withdrawn third ground of rejection), the sole basis of rejection of this claim currently in the application is the first ground of rejection identified by the Applicant.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

No evidence is relied upon by the examiner in the rejection of the claims under appeal.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 16, 18, and 34-36 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The sole ground of rejection identified by the Appellant, and recognized as a rejection currently at issue, is that the application does not provide adequate descriptive support for the claimed genus of antibodies that bind a two-chain (active) form of the protein identified as matriptase with greater affinity than a one-chain (inactive) form of the protein.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the Appellant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the Appellant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed, although it may also be found by the provision of a functional in combination with structure correlating thereto.

As indicated above, the present claims are drawn to a genus of antibodies that preferentially bind to the two-chain form of matriptase over the single chain form. The basis of the rejection is not that there is insufficient support for a genus of antibodies that bind to the matriptase protein. Rather, the rejection is on the ground that there is insufficient support to demonstrate possession of the subset of such antibodies that are required to have the additional functional limitation of being able to distinguish between the two forms (active and inactive) of the protein. Thus, the rejected claims are directed to antibodies with specificity for specific epitopes (linear or conformational) that give the claimed antibodies specificity for one form of matriptase over the other.

In view of the fact that the claims are not directed to anti-matriptase antibody, but to a particular subset thereof, the mere identification of the target antigen is not sufficent to describe the present antibodies as these antibodies are being required to distinguish between two versions of the same protein. In this case, in order to fully characterize the target antigen, the application must provide some structural means by which the antibodies could distinguish between the two forms of the protein. This could be done, for example, by identifying structures or epitopes that are present or displayed in the two-chain form that are not present or displayed on the single chain form. No such structural features have been provided.

It is noted that the application does provide two examples of antibodies that bind to the two-chain human matriptase with greater affinity than to the single chain form: the M123 and M69 antibodies. It is also noted that when the rejection was originally made, there were certain defects relating to the deposit rules with respect to the Appellant's disclosure of these antibodies. These defects have since been corrected as indicated by the withdrawal of the enablement rejection of claims 15 and 19 in the Advisory action of November 30, 2005. However, while the application discloses these antibodies, it has not provided any means of determining what epitope[s] these antibodies target so as to allow those in the art identify and particular structure that may be targeted which structure would correspond to an epitope present in the two-chain but not in the single-chain form of matriptase.

In addition, even if the epitopes bound by these antibodies had been identified, such identification would provide little description relevant to determining what other epitopes may be targeted to achieve the same function. The Courts have stated that the presence of multiple species with in a claimed genus does not necessarily demonstrate possession of the genus "where

there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated." See, *In re Smyth*, 178 U.S.P.Q. 279 at 284-85 (CCPA 1973); and *University of California v. Eli Lilly* and Co., 43 USPQ2d 1398, at 1405 (Fed Cir 1997)(citing Smyth for support). See also, *Noelle v. Lederman*, 69 U.S.P.Q.2d 1508, at 1514 (CAFC 2004) (specifically applying the uncertainty rational to an antibody fact pattern). In the present case, the disclosure of these two antibodies provides no information as to the identification of other antibodies within the claimed genus. These two disclosed antibodies fail to provide any additional information as to what epitopes or structures are present in the two-chain form that are not present on the single-chain form of matriptase, or as to what other antbodies would be capable of distinguishing between the two forms of the protein. Thus, disclosure of these antibodies provides no certainty as to the ability of other antibodies to similarly distinguish between the two forms of matriptase. In view of this lack of certainty, the disclosure of these antibodies fails to provide adequate support for the claimed genus.

Thus, the present application does not provide adequate written description support for the claimed genus of antibodies in either the form of a representative number of species, or of a full characterization of the targeted antigen. Claims 16, 18, and 34-36 have therefore been rejected as lacking adeuate written description support.

(10) Response to Argument

The Appellant traverses the rejection of claims 16, 18, and 34-36 above on three grounds.

First, the Appellant argues that the rejection is improper on the grounds that they have identified the target antigen, matriptase, by its sequence. In support of this argument, Appellant notes that the PTO's Guidelines for determining written description provides an example

indicating that mere identification of the target antigen provides adequate support for antibodies that bind thereto. While this is a correct analysis of the referenced example, it is not a proper analogy in this case.

The example in the guidelines is based on consideration of a claim "directed to an antibody that is capable of binding to antigen X." As was indicated above, and unlike the example in the guidelines, the present claims are not merely drawn to an antibody that binds to the target antigen. Instead, the present claims are drawn to a subgenus of such antibodies that is further defined by the ability to distinguish between the single-chain (inactive) and the two-chain (active) forms of the protein. Thus, unlike in situations were an antibody merely has to bind a target protein, the presently claimed subgenus of antibodies must be characterized so as to demonstrate possession of this specific subgenus separately from the larger genus of anti-matriptase antibodies.

Appellant asserts that they have disclosed and characterized the target antigen. Such would be sufficient for claims drawn to anti-matriptase antibodies generally. However, the characteristics identified on page 10 of the Brief on Appeal do not aid in determining what antibodies will and will not be capable of distinguishing between the two forms of the protein as required by the claimed subgenus.

The Appellant further asserts that the application "demonstrates that the two-chain form of human matriptase is structurally and functionally distinct from the single-chain form." However, while the application has demonstrated that the two forms *are distinct*, the application does not define *how they are distinct* in a manner relevant to the identification of antibodies that distinguish between the two forms (e.g., through identification of structures or epitopes present

or accessible to antibodies in one form but not the other). Thus, while Appellant's reference to Patent Office's Guidelines are pertinent to the current claims, they should not be considered conclusive in view of the differences between the facts of the present case and the facts provided in the Guidelines' example. This first argument should therefore not be found persuasive.

Appellant next asserts that support for the claimed genus may be found in the Appellant's description of "reliable screening and assay procedures" that can be used to identify other antibodies. However, the disclosure of such an assay is not descriptive of the antibodies that may be so identified. See e.g., University of Rochester v. G.D. Searle & Co., 69 U.S.P.Q.2d 1886, at 1895 (CAFC 2004). Moreover, it is noted that while the Appellant successfully identified at least 2 representative antibodies (after several layers of screening), there is no indication as to how many times the process as a whole had to be run to identify these antibodies. The application and arguments indicate only that over 80 hybridoma clones were identified. There are no teachings to indicate how many tests were run to identify these 80 clones. Thus, it is not clear that each time that the disclosed processes and assays are run at least one of the indicated antibodies would be identified, particularly where only two antibodies were identified that bind preferentially to the two-chain form over the single chain form of matriptase. This argument also should therefore not be found persuasive.

Appellant's third argument asserts that the two identified antibodies are sufficiently representative to provide support for the claimed genus of antibodies. This argument should not be found persuasive for the reasons indicated in the statement of the rejection above. I.e., these

antibodies are not representative of the claimed genus in that they provide no indication as to what other antibodies would have the required binding characteristics. This is particularly the case in view of the uncertainty as to the identification of such other antibodies, as shown by the Appellant's indication that only 2 of 80 produced hybridomas provide antibodies with the requisite function.

None of the Appellant's three arguments should therefore be found persuasive in overcoming the written description rejection as described above.

It is noted that additional arguments have been provided. For example, on pages 13-14, Appellant presents arguments directed to claim 18, which is drawn to antibodies with the required function that are monoclonal antibodies. This claim is not separately rejected. It is conceded that, if the Appellant were found to have adequate descriptive support for the subgenus as described above, Appellant would also have adequate support for the monoclonal antibodies of claim 18.

The remaining arguments address what the Appellant identified as the Second, Third, and Fourth grounds of rejection. Of these, the second ground of rejection was withdrawn in the Advisory action of November 30, 2005 in view of the declaration referenced in the argument; the Third ground of rejection is moot in view of the amendments to claim 36 in the After-Final amendment of November 8, 2005; and the Fourth ground of rejection was not made. While the Examiner notes that a sentence of page 8 of the Final rejection of August 10, 2005 could have been interpreted as a rejection of claim 36 on the basis that the antibodies do not have the function of HAI-1; in fact, the statement was intended to convey only that the M123 antibody

failed to provide adequate support for the claimed genus of antibodies addressed in the first ground of rejection above.

None of these additional arguments address, and should therefore not be found persuasive with respect to, the first ground of rejection described above.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Zachariah Lucas
Patent Examiner, AU 1648

Conferees:

Bruce R. Campell
Supervisory Patent Examiner, AU 1648

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER

Jeffery Siew
Supervisory Patent Examiner, AU 1645